2-Chloronitrobenzene

CAS #88-73-3
Swiss CD-1 mice, at 0.0, 40, 80, and 160 mg/kg, gavage
Robert Chapin, NTP/NIEHS Project Officer
Dushyant Gulati, Linda Grimes, and Leta Barnes,
Environmental Health Research and Testing
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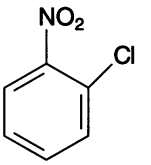

2-Chloronitrobenzene (2CNB), a widely used chemical intermediate, was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol, based on an indication of reduced sperm motility after inhalation exposure in B6C3F1 mice, and because 2CNB is a nitroaromatic, a class of compounds containing many reproductive toxicants. Chloronitrobenzenes also induce methemoglobinemia, which reduces red cell cycle time and increases red cell clearance, producing a subsequent increase in spleen weight. Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 0.0, 40, 80, and 160 mg/kg by gavage in corn oil.

In the F_0 generation (Task 2) animals, there was a slight (3–6%) increase in sire weights and postpartum dam weights in the high dose group. Four, two, two, and three mice died in the control to high dose groups, respectively; the variety of causes of death suggests that these deaths were not directly related to 2CNB exposure. Three females in the high dose group appeared cyanotic during the holding period at the end of Task 2; otherwise, there were no significant clinical signs.

2CNB exposure caused no decrement in reproductive function in the F_0 mice: the number of litters, pup weight and viability were all unchanged. The number of live pups per litter was increased (15%) in the high dose group, a finding of questionable biological significance.

The last litter from all dose groups was reared by the dam until weaning. Pup viability was unaffected by maternal 2CNB exposure, although pup body weights at weaning were reduced at all dose levels by approximately 10 to 13%.

In the absence of any adverse reproductive effects in Task 2, the Task 3 crossover mating trial was not conducted. After the last litter from Task 2 was weaned, 12 control and high dose mice were killed and samples for spleen weight and methemoglobin were collected. Relative spleen weight was increased by 50 to 100%, while methemoglobin levels were increased 4- to 6-fold. No other necropsy data were collected.

The Task 4 mating trial used only the control and high dose groups. There was no difference between the groups in terms of proportion of mated pairs, number of litters per group, number of live pups per litter, or pup weight or viability.

After the F_2 pups were delivered and evaluated, the F_1 adults were killed and necropsied. The treated males were approximately 7% heavier than their control counterparts, while relative liver and spleen weights were increased by approximately 40 and 60%, respectively. Relative seminal vesicle weight was reduced by approximately 7%; sperm measured were unchanged. Female body weight was increased by approximately 5%, while relative liver and spleen weights were increased by approximately 40% each. Estrous cycle measures were unchanged by 2CNB exposure. Methemoglobin was increased approximately 3-fold in the treated animals.

Thus, 2-chloronitrobenzene was without reproductive toxicity in the presence of significant changes in liver and spleen weight and with elevated methemoglobin levels.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB92187608/AS**
Chemical: **2-Chloronitrobenzene**
CAS#: **88-73-3**
Mode of exposure: **Gavage (corn oil vehicle)**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	40 mg/kg	80 mg/kg	160 mg/kg
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, ↑	—, ↑
Kidney weight[a]	•	•	↑, ↑
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	•	•	•
Water consumption	—, —	—, —	—, —
Clinical signs	—, —	—, —	—, ↑
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	↑, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	•	•	160 mg/kg
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	—, ↓	↓, ↓	↓, ↓
Mortality	—, —	—, —	—, —
Adult body weight	•	•	↑, ↑
Kidney weight[a]	•	•	—, —
Liver weight[a]	•	•	↑, ↑
Feed consumption	•	•	•
Water consumption	•	•	—, —
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, —
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, ↓
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Neither
Study confounders:	None
NOAEL reproductive toxicity:	80 mg/kg
NOAEL general toxicity:	<40 mg/kg
F_1 more sensitive than F_0?	No
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.